## **CLAIMS:**

5

10

15

20

30

1. Use of a compound or a composition comprising said compound for inhibiting the activity of at least one kinase, other than ROCK kinase, *in vitro* or *in vivo*, wherein said compound is a compound of the formula (I):

$$[Ring(1)] \longrightarrow Rb$$

$$[Ring (3)] \longrightarrow [C(R_1)(R_2)]_n \longrightarrow Rc$$

$$(I)$$

(wherein:

Ring (1) is a substituted or unsubstituted, saturated, unsaturated or aromatic 4-, 5-, 6-, 7- or 8-membered ring containing carbon atoms and at least one hydrogen-accepting heteroatom and optionally 1 or 2 further heteroatoms;

 $R_a$  is a hydrogen or a linear or branched, substituted or unsubstituted  $C_1$ - $C_6$  alkyl, substituted or unsubstituted  $C_1$ - $C_6$  alkoxy or substituted or unsubstituted aryl;

Ring (3) is a substituted or unsubstituted, saturated, unsaturated or aromatic 4-, 5-, 6-, 7- or 8-membered ring containing carbon atoms and optionally 1 or 2 heteroatoms;

each  $R_1$  or  $R_2$ , may be the same or different, and is independently selected from the group consisting of hydrogen, a substituted or unsubstituted, saturated, unsaturated or aromatic 3-, 4-, 5-, 6-, 7- or 8- membered ring containing carbon atoms and optionally one or two heteroatoms, substituted or unsubstituted  $C_1$ - $C_6$  alkyl or cyano;

n is 0, 1 or 2; and

 $R_b$  and  $R_c$  are such that the amino group -NR<sub>b</sub>R<sub>c</sub> is essentially in a protonated form at a pH between 5.0-9.0;

and wherein:

(1) the group R<sub>a</sub>, the nitrogen atom to which group R<sub>a</sub> is bound, the carbon atom of Ring (1) to which the N-R<sub>a</sub> nitrogen atom is bound, and one carbon atom of Ring (1) adjacent to the carbon atom of Ring (1) to which the N-R<sub>a</sub> nitrogen atom is bound may form Ring (7) wherein Ring (7) is a substituted or unsubstituted, saturated, unsaturated or aromatic 4-, 5- or 6- membered ring that contains carbon atoms, the N-R<sub>a</sub> nitrogen atom and optionally one further heteroatom chosen from oxygen, sulfur and nitrogen;

5

10

15

20

25

- (2) where Ring (3) is a 1,4-phenylene group, one of  $R_1$  and  $R_2$ , the carbon atom to which  $R_1$  and  $R_2$  are bound and two of the carbon atoms belonging to the 1,4-phenylene group may form a substituted or unsubstituted 5-, 6-, 7- or 8- membered ring that contains carbon atoms, the nitrogen atom of the amino group  $NR_bR_c$  and optionally one further heteroatom chosen from oxygen, sulfur and nitrogen and that may be saturated or contain one double bond;
- (3) where Ring (3) is a 1,4-phenylene group, one of  $R_b$  or  $R_c$ , the nitrogen atom to which  $R_b$  or  $R_c$  are bound, the carbon atom to which  $R_1$  or  $R_2$  are bound and two of the carbon atoms belonging to the 1,4-phenylene group may form a substituted or unsubstituted 5-, 6-, 7- or 8- membered ring that contains carbon atoms, the nitrogen atom of the amino group  $-NR_bR_c$  and optionally one further heteroatom chosen from oxygen, sulfur and nitrogen and that may be saturated or contain one double bond;
- one of  $R_b$  and  $R_c$  may, together with the nitrogen atom of the amino group  $-NR_bR_c$ , one of  $R_1$  and  $R_2$  and the carbon atom to which  $R_1$  and  $R_2$  are bound, form a substituted or unsubstituted 5-, 6-, 7- or 8- membered ring that contains carbon atoms, the nitrogen atom of the amino group  $-NR_bR_c$  and optionally one further heteroatom chosen from oxygen, sulfur and nitrogen and that may be saturated or contain one double bond; and
- (5)  $R_b$ ,  $R_c$  and the nitrogen atom to which they are bound may together from a substituted or unsubstituted ring with between 3 and 10, preferably between 4 and 7, and most preferably 5 or 6 atoms in the ring (including the nitrogen atom to which both  $R_a$  and  $R_b$  are bound) so that the ring so formed consists of a nitrogen atom, carbon atoms and optionally one further heteroatom chosen from oxygen, nitrogen and sulfur; and wherein:
- the distance between the at least one hydrogen-accepting heteroatom in Ring (1) and the  $N(R_a)(R_b)$  nitrogen atom, as determined using a Scatter Plot, is in the range of 11.0 to 11.8 Angstrom),

or a salt, or pro- or predrug thereof.

30 2. Use as claimed in claim 1 wherein:

 $R_a$  is hydrogen, a linear or branched, substituted or unsubstituted  $C_1$ - $C_6$  alkyl, substituted or unsubstituted  $C_1$ - $C_6$  alkoxy or substituted or unsubstituted aryl; or the group  $R_a$ , the nitrogen atom to which group  $R_a$  is bound, the carbon atom of Ring (1) to which the N- $R_a$  nitrogen atom is bound, and one carbon atom of Ring (1) adjacent to the

WO 2005/082367 PCT/IB2005/000600

5

10

15

25

30

carbon atom of Ring (1) to which the N-R<sub>a</sub> nitrogen atom is bound may form Ring (7) wherein Ring (7) is a substituted or unsubstituted, saturated, unsaturated or aromatic 4-, 5- or 6- membered ring that contains carbon atoms, the N-R<sub>a</sub> nitrogen atom and optionally one further heteroatom chosen from oxygen, sulfur and nitrogen;

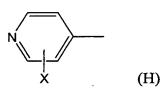
- 90 -

- $[C(R_1)(R_2)]_n$ -NR<sub>a</sub>R<sub>b</sub> is an alkylene amino group, in which said amino group is a primary or secondary amino group.
- 3. Use as claimed in claim 2 wherein R<sub>a</sub> is hydrogen, a linear or branched, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl or the group R<sub>a</sub>, the nitrogen atom to which group R<sub>a</sub> is bound, the carbon atom of Ring (1) to which the N-R<sub>a</sub> nitrogen atom is bound, and one carbon atom of Ring (1) adjacent to the carbon atom of Ring (1) to which the N-R<sub>a</sub> nitrogen atom is bound may form Ring (7) wherein Ring (7) is a substituted or unsubstituted, saturated, unsaturated or aromatic 4-, 5- or 6- membered ring that contains carbon atoms, the N-R<sub>a</sub> nitrogen atom and optionally one further heteroatom chosen from oxygen, sulfur and nitrogen.
  - 4. Use as claimed in any one preceding claim wherein the amino group  $-NR_bR_c$  is essentially in a protonated form at a pH of between 6.0 and 8.0.
- 5. Use as claimed in any one preceding claim wherein the amino group -NR<sub>b</sub>R<sub>c</sub> is essentially in a protonated form at a pH of about 7.
  - 6. Use as claimed in any one preceding claim wherein the distance between the at least one hydrogen-accepting heteroatom in Ring (1) and the  $N(R_a)(R_b)$  nitrogen atom, as determined using a Scatter Plot, is in the range of 11.0 to 11.6 Angstrom.
  - 7. Use as claimed in any one preceding claim wherein the distance between the at least one hydrogen-accepting heteroatom in Ring (1) and the  $N(R_a)(R_b)$  nitrogen atom, as determined using a Scatter Plot, is in the range of 11.0 to 11.4 Angstrom.
  - 8. Use as claimed in any one preceding claim wherein the at least one hydrogen-accepting heteroatom in Ring (1) is a nitrogen atom.
  - 9. Use as claimed in any one preceding claim wherein Ring (1)- is of formula (H):

5

15

20



wherein -X may be absent or denotes substitution with 1-4 substituents X that are independently chosen from halogen,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, substituted or unsubstituted aryl, nitro, hydroxyl and a substituted or unsubstituted amino group.

- 10. Use as claimed in claim 9 wherein -X denotes substitution with 1 or 2 substituents X.
- 10 11. Use as claimed in any one of claims 1 to 10 wherein Ring (1)- is of formula (A):

wherein, independently in each ring shown in Formula V, -X may be absent or denotes substitution with 1 or 2 substituents X that are independently chosen from halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, substituted or unsubstituted aryl, nitro, hydroxy and a substituted or unsubstituted amino group.

12. Use as claimed in any one preceding claim wherein -Ring (3)- is the group (L):

- wherein -Y may be absent or denotes substitution with 1-4 substituents Y that are independently chosen from halogen,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, substituted or unsubstituted aryl, nitro, hydroxy and an amino group.
- 13. Use as claimed in claim 12 wherein -Y denotes substitution with 1 or 2 substituents Y.

5

10

15

20

30

14. Use as claimed in any one preceding claim wherein:
n=1:

one of  $R_1$  or  $R_2$  is hydrogen and the other one is chosen from the group consisting of: hydrogen, substituted or unsubstituted, saturated, unsaturated or aromatic, 3-, 4-, 5-, 6-, 7- or 8- membered ring containing carbon atoms and optionally one or two heteroatoms, cyano, substituted or unsubstituted  $C_1$ - $C_6$  alkyl;

one of  $R_b$  and  $R_c$  is hydrogen and the other one is chosen from the group consisting of hydrogen, substituted or unsubstituted  $C_1$ - $C_{10}$  alkyl;

where Ring (3) is a 1,4-phenylene group, one of  $R_1$  and  $R_2$ , the carbon atom to which  $R_1$  and  $R_2$  are bound and two of the carbon atoms belonging to the 1,4-phenylene group may form a substituted or unsubstituted 5-, 6-, 7- or 8- membered ring that contains carbon atoms, the nitrogen atom of the amino group  $NR_bR_c$  and optionally one further heteroatom chosen from oxygen, sulfur and nitrogen and that may be saturated or contain one double bond; and

where Ring (3) is a 1,4-phenylene group, one of  $R_b$  or  $R_c$ , the nitrogen atom to which  $R_b$  or  $R_c$  are bound, the carbon atom to which  $R_1$  or  $R_2$  are bound and two of the carbon atoms belonging to the 1,4-phenylene group may form a substituted or unsubstituted 5-, 6-, 7- or 8- membered ring that contains carbon atoms, the nitrogen atom of the amino group  $-NR_bR_c$  and optionally one further heteroatom chosen from oxygen, sulfur and nitrogen and that may be saturated or contain one double bond.

- 15. Use as claimed in claim 14 wherein one of  $R_1$  or  $R_2$  is hydrogen and the other one is substituted or unsubstituted aryl.
- Use as claimed in claim 14 or claim 15 wherein both  $R_b$  and  $R_c$  are hydrogen.
  - 17. Use as claimed in claim 1 wherein said compound is chosen from the group comprising (R)-(+)-trans-N-(4-pyridyl)-4-(1-aminoethyl)-cyclohexanecarboxamide; trans-4-aminomethyl-cyclohexanecarboxylic acid pyridin-4-ylamide; 4-aminomethyl-N-pyridin-4-yl-benzamide; 5-(1-amino-ethyl)-thiophene-2-carboxylic acid pyridin-4-ylamide; 4-(1-amino-ethyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-propyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-3,3-dimethyl-butyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-cyclopentyl-methyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-cyclopentyl-methyl-neth

cyclohexyl-methyl)-N-pyridin-4-yl-benzamide; 1,2,3,4-tetrahydro-isoquinoline-6carboxy-pyridin-4-yl-amide; N-pyridin-4-yl-4-pyrrolidin-2-yl-benzamide; 4-piperidin-2yl-N-pyridin-4-yl-benzamide; 1,2,3,4-tetrahydro-isoquinoline-6-carboxylic acid pyridin-4-yl-amide; 4-(4,5-dihydro-1H-imidazol-2-yl)-N-pyridin-4-yl-benzamide; N-pyridin-4-yl-4-(1,4,5,6-tetrahydro-1H-pyrimidin-2-yl)-benzamide; 4-(1-amino-phenyl-methyl)-N-5 pyridin-4-yl-benzamide; 4-[1-amino-(4-fluorophenyl)-methyl]-N-pyridin-4-yl-benzamide; 4-[1-amino-(4-methoxyphenyl)-methyl]-N-pyridin-4-yl-benzamide; 4-(1-amino-ethyl)naphthalene-1-carboxylic acid pyridin-4-ylamide; 4-aminomethyl-2,5-dimethyl-Npyridin-4-yl-benzamide; 5-(1-amino-ethyl)-thiophene-2-carboxylic acid N-(1Hpyrrolo[2,3-b]pyridin-4-yl)-benzamide; 4-(1-amino-ethyl)-N-(1H-pyrrolo[2,3-b]pyridin-10 4-yl)-benzamide; 4-(1-amino-cyclopentyl-ethyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)benzamide; 1,2,3,4-tetrahydro-isoquinoline-6-carboxylic acid -N-(1H-pyrrolo[2,3b]pyridin-4-yl)-benzamide; 4-piperidin-2-yl-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)benzamide; 4-(1-amino-cyclobutyl-ethyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-2,2-15 dimethyl-butyl)-N-pyridin-4-yl-benzamide; 1-amino-indan-5-carboxylic acid pyridin-4yl-amide; 4-(1-amino-butyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-pentyl)-N-pyridin-4yl-benzamide; 4-(1-amino-2-methyl-propyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-2,2dimethyl-propyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-propyl)-N-(1H-pyrrolo[2,3b]pyridin-4-yl)-benzamide; 4-(1-amino-cyclopropyl-ethyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-benzamide; 4-(1-amino-cyclobutyl-ethyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-20 benzamide; 4-(1-amino-2,2-dimethyl-butyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)benzamide; 1-amino-indan-5-carboxylic acid (1H-pyrrolo[2,3-b]pyridin-4-yl)-amide; 5amino-5,6,7,8-tetrahydro-naphthalene-2-carboxylic acid (1H-pyrrolo[2,3-b]pyridin-4-yl)amide; 4-(1-amino-butyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-benzamide and 4-(1-amino-2,2-dimethyl-propyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-benzamide. 25

18. Use as claimed in claim 1 wherein said compound is chosen from the group comprising 4-(1-amino-ethyl)-*N*-pyridin-4-yl-benzamide; 4-(1-amino-propyl)-*N*-pyridin-4-yl-benzamide; 4-(1-amino-cyclopropyl-ethyl)-*N*-pyridin-4-yl-benzamide; 4-(1-amino-cyclopentyl-methyl)-*N*-pyridin-4-yl-benzamide; 4-(1-amino-cyclopentyl-methyl)-*N*-pyridin-4-yl-benzamide; 1,2,3,4-tetrahydro-isoquinoline-6-carboxy-pyridin-4-yl-amide; *N*-pyridin-4-yl-4-pyrrolidin-2-yl-benzamide; 4-piperidin-2-yl-*N*-pyridin-4-yl-benzamide; 4-(1-amino-phenyl-methyl)-*N*-pyridin-4-yl-benzamide; 4-[1-amino-(4-fluorophenyl)-methyl]-*N*-

30

WO 2005/082367 PC

- 94 -

PCT/IB2005/000600

pyridin-4-yl-benzamide; 4-(1-amino-ethyl)-naphthalene-1-carboxylic acid pyridin-4ylamide; 4-aminomethyl-2,5-dimethyl-N-pyridin-4-yl-benzamide; 5-(1-amino-ethyl)thiophene-2-carboxylic acid N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-benzamide; 4-(1-aminoethyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-benzamide; 4-(1-amino-cyclopentyl-ethyl)-N-(1*H*-pyrrolo[2,3-*b*]pyridin-4-yl)-benzamide; 1,2,3,4-tetrahydro-isoquinoline-6-carboxylic acid -N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-benzamide; 4-piperidin-2-yl-N-(1H-pyrrolo[2,3b]pyridin-4-yl)-benzamide; 4-(1-amino-cyclobutyl-ethyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-2,2-dimethyl-butyl)-N-pyridin-4-yl-benzamide; 1-amino-indan-5-carboxylic acid pyridin-4-yl-amide; 4-(1-amino-butyl)-N-pyridin-4-yl-benzamide; 4-(1-aminopentyl)-N-pyridin-4-yl-benzamide; 4-(1-amino-2-methyl-propyl)-N-pyridin-4-ylbenzamide; 4-(1-amino-2,2-dimethyl-propyl)-N-pyridin-4-yl-benzamide; 4-(1-aminopropyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-benzamide; 4-(1-amino-cyclopropyl-ethyl)-N-(1H-pyrrolo[2,3-b]pyridin-4-yl)-benzamide; 4-(1-amino-cyclobutyl-ethyl)-N-(1Hpyrrolo[2,3-b]pyridin-4-yl)-benzamide; 4-(1-amino-2,2-dimethyl-butyl)-N-(1Hpyrrolo[2,3-b]pyridin-4-yl)-benzamide; 1-amino-indan-5-carboxylic acid (1Hpyrrolo[2,3-b]pyridin-4-yl)-amide; 5-amino-5,6,7,8-tetrahydro-naphthalene-2-carboxylic acid (1H-pyrrolo[2,3-b]pyridin-4-yl)-amide; 4-(1-amino-butyl)-N-(1H-pyrrolo[2,3b]pyridin-4-yl)-benzamide and 4-(1-amino-2,2-dimethyl-propyl)-N-(1H-pyrrolo[2,3b]pyridin-4-yl)-benzamide.

20

10

15

- 19. Use according to any one preceding claim wherein said use is *in vitro*.
- 20. Use according to any one preceding claim wherein the at least one kinase is chosen from the isoforms of Protein Kinase C.

25

- 21. Use according to claim 20 in which the at least one kinase is chosen from the calcium-independent, but diacylglycerol- and/or phorbol ester-sensitive isoforms of PKC.
- 22. Use according to claim 21 in which the at least one kinase is chosen from the epsilon and/or theta isoforms of Protein Kinase C.
  - 23. Use of a compound as defined in any of claims 1 to 18 in the preparation of a medicament for the prevention and/or treatment of at least one disease and/or disorder selected from the group comprising metabolic diseases, anxiety, addiction, withdrawal

symptoms, muscle spasms, convulsive seizures, epilepsy, pain, cardiovascular disease and heart disease; and/or for regulating the immune system and/or an immune response and/or inflammatory response in a mammal.

24. Use according to claim 23 wherein said metabolic disease or disorder is at least one of the following:

hyperglycemic conditions and/or other conditions and/or diseases that are (primarily) associated with (the response or sensitivity to) insulin, such as Type I and Type II diabetes, severe insulin resistance, hyperinsulinemia, hyperlipidemia, and insulinresistant diabetes, such as Mendenhall's Syndrome, Werner Syndrome, leprechaunism and lipoatrophic diabetes, and other lipoatrophies;

obesity;

5

10

15

25

30

conditions caused or usually associated with hyperglycemic conditions and/or obesity, such as hypertension, osteoporosis and/or lipodystrophy; or

metabolic syndrome;

as well as various inherited metabolic diseases known per se; and may also be used also for preventing, treating and/or alleviating complications and/or symptoms associated with these metabolic diseases.

- 25. Use of a compound as defined in any of claims 1 to 18 for the preparation of a medicament for the prevention and/or treatment of type II diabetes, and/or for preventing, treating and/or alleviating complications and/or symptoms associated therewith.
  - 26. Use of a compound as defined in any of claims 1 to 18 for the preparation of a medicament for the prevention and/or treatment of obesity, and/or for preventing, treating and/or alleviating complications and/or symptoms associated therewith.
    - 27. Use of a compound as defined in any of claims 1 to 18 for the preparation of a medicament for the prevention, treatment and/or management of pain, and/or for preventing, treating and/or alleviating complications and/or symptoms associated therewith.
    - 28. A pharmaceutical and/or veterinary composition containing a compound as defined in any of claims 1 to 18.

WO 2005/082367 PCT/IB2005/000600

- 96 -

29. A pharmaceutical and/or veterinary composition as claimed in claim 28 comprising at least one compound according to any one of claims 1 to 18 and at least one carrier, excipient or diluent acceptable for pharmaceutical and/or veterinary purposes.

30. A compound as defined in any one of claims 1 to 18 for use in human or veterinary medicine.

31. A compound as defined in any one of claims 1 to 18.

5

10